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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,931	07/26/2001	Hilton A. Salhanick	62694-A/JPW/SHS	8253

7590 11/13/2006

Cooper & Dunham, LLP  
1185 Avenue of the Americas  
New York, NY 10036

EXAMINER
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DAVIS, DEBORAH A

ART UNIT	PAPER NUMBER
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1655

DATE MAILED: 11/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/915,931

Applicant(s)

SALHANICK ET AL.

Examiner

Deborah A. Davis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 31 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 136-152 and 155 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 136-152 and 155 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicants' response to the Office Action mailed on February 24, 2006 has been acknowledged. Currently, claims 136-152 and 155 are pending.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 136-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view Yoshida (Endocrinology, Japon, 1988, Vol. 35, No. 5, pages 733-799 in view of Shuurs et al (USP#4,016,043).

A method of diagnosing a thyroid condition in a subject is by obtaining a suitable unconcentrated urine sample from the subject; and determining the concentration of thyroid stimulating hormone in the sample by a method which is not a radioimmunoassay wherein a concentration of thyroid stimulating hormone corresponding to greater than about 0.35 uIU/ml in the subject's urine, as determined using the WHO reference standard WO 80/58, diagnoses hypothyroidism in the subject; and a concentration of thyroid stimulating hormone less than about 0.04 uIU/ml in the subject's urine as determined using the WHO reference standard WO 80/558 diagnoses hyperthyroidism in the subject is apparently claimed.

The cited reference of Yoshida et al teaches a method of measuring TSH (thyroid stimulating hormone) in unprocessed (i.e. unconcentrated) urine from normal subjects, primary hypothyroidism and renal disease. The urine TSH results were compared with serum TSH results concentration. The method of measuring TSH in urine was performed with an immunoradiometric assay kit that allows detection of levels down to 0.03 uU TSH/ml. Coated beads with antibodies (i.e. an agent capable of binding to TSH) were incubated with human followed with was steps and TSH was measured with a gamma counter (see for example page 734 - materials and methods) as claimed. The antibodies were labeled with detectable markers.

Yoshida et al does not teach the exclusion of radioimmunoassay when measuring TSH in urine.

However, Schuurs et al teaches the disadvantages of using a radioimmunoassay in that although they are sensitive, the requirement of special equipment, trained staff, the need for extra safety measures to protect against and the short half-life span of the radioactive labeling element. The possibility of replacing the radioactive label with an enzyme label is proposed (col. 1, lines 25-42).

It would have been obvious to one of ordinary skill in the art to want to modify the teaching of Yoshida to exclude using an radioimmunoassay and replace it with EIA as taught by Schuurs et al for extra safety measures when using radioactive products in a laboratory setting. Further, the exclusion of using radioactive products requires less disposal time, while the Enzyme Immunoassay provides a very simple, and sensitive assay method. With respect to the TSH measurements of indicated hypothyroidism and

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hyperthyroidism, it is noted that the prior art has already established that low levels indicates hyperthyroidism while higher are indicative of hypothyroidism. Absent the evidence to the contrary, applicant's claims are directed to the same premise.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of the evidence to the contrary.

Claims 142-152 and 155 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al, in view of Schuurs in view of Philo et al (USP#5,108,896) and in further view of Orden et al (Acta Endocrinologica (Copenh) 1987, Vol. 114, pages 503-508.

The teaching of Yoshida et al in view of Schuurs et al are set forth above and differ from the instant claims in not teaching thyroxine in unconcentrate urine and dual detection of hormones (i.e. TSH and thyroxine).

The cited teaching of Orden et al beneficially teaches that thyroxine can be measured in unextracted urine (i.e. unconcentrated) and is a good indicator of thyroid function (i.e. euthyroid, hypothyroid and hyperthyroid, see for example abstract and table 1).

The cited reference of Philo et al beneficially teaches a dual analyte enzyme immunoassay for assaying two antigens in a single sample wherein reactions occur simultaneously (see abstract). Philo teaches that immunoassays of the present invention are particularly advantageous for assaying pairs of antigens that are found together in physiological samples such as human serum or urine samples. Labels

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utilized in the instant assay are fluorescein, rhodamine, isothiocyanate and others (col. 7, lines 12-25). Such immunoassays systems are desirable for assaying pairs of hormones including Thyroxine (T4)/ Thyroid Stimulating Hormone (TSH) and others (col. 4, lines 27-36).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further include measuring the concentration of Thyroxine (T4) because this hormone is found together with TSH in biological samples such as urine and blood. One skilled in the art would want to measure TSH and Thyroxine in one assay system because if TSH measurements appear discordant with clinical thyroid evaluations, Thyroxine measurements are helpful for identifying inaccurate TSH measurements. One would be motivated to measure both hormones because dual measurements of TSH/Thyroxine can reduce the time required to run each test separately. With respect to the Thyroxine and TSH measurements of indicated hypothyroidism and hyperthyroidism, it is noted that the prior art has already established that low levels indicates hyperthyroidism while higher are indicative of hypothyroidism. Further, one skilled in the art would be motivated to measure thyroxine in unconcentrated urine to eliminate purification steps wherein the sample can be assayed upon collection, reducing the time required to perform the assay. Absent the evidence to the contrary, applicant's claims are directed to the same premise.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of the evidence to the contrary.

### ***Response to Arguments***

Applicant's arguments, see pages 4-6, filed, with respect to the rejection(s) of claim(s) 136-152 and 155 under 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Yoshida et al in view of Shuurs. Also 103(a) rejection in view of Yoshida et al, Schuurs, Philo et al and in further view of Orden et al.

Applicant argues that the reference of Philo et al or Shuurs et al fails to teach urinary TSH and/or Thyroxine can be measured in unconcentrated urine and reliably detect hypothyroidism and hyperthyroidism.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

### ***Conclusion***

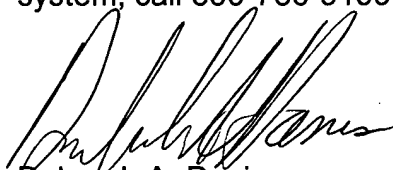
No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A. Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, McKelvey Terry can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Deborah A. Davis  
Patent Examiner  
Art Unit 1655  
October 2006



CHRISTOPHER R. TATE  
PRIMARY EXAMINER